REMARKS

Formal Matters

Applicants thank the Examiner for the interview of June 16, 2003. Applicants have amended claims 1-4 and 9, and added new claims 15 and 16. Applicants have also canceled claims 5-8 and 13. Support for the new claims may be found in, for example, original claims 3-5. Therefore, no new matter has been added.

Applicants acknowledge the Examiner's withdrawal of the 35 U.S.C. § 112, second paragraph rejection of claim 2.

Claims 1-4, 9-12, 15, and 16 are now pending in this application.

Obviousness Rejection

The Office has rejected claims 1-3 and 5-13 under 35 U.S.C. § 103(a) as "being unpatentable over Hao et al. (Human Gene Therapy (July 1995) 6: 873-880) in view of Uzan et al. (J. Biol. Chem. (1991) 266(14): 8932-8939) and Romp et al. (Blood Coagulation and Fibrinolysis (1993) 4:905-910)." Office Action at page 3. Further, the Office rejected claim 4 under 35 U.S.C. § 103(a) as being unpatentable over Hao et al., Uzan et al, and Romp and further in view of Kurachi et al. (J. Biol. Chem. (1995) 279(10):5276-5281). *See* Office Action at page 8. Claims 5-8 are cancelled and, therefore, the rejection as to these claims is moot.

Applicants maintain that the Office has failed to establish a *prima facie* case of obviousness because a skilled artisan would not reasonably expect to succeed in

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expressing Factor IX in hematopoietic cells using a hematopoietic-specific promoter if he were to combine Hao, Romp, and Uzan. Hao merely speculates as to the possibility of targeting Factor IX expression to a specific lineage. (Hao; page 879, left column, second paragraph.) However, there is no guidance as to what specific hematopoietic cell types should be targeted or whether any specific hematopoietic cell type would successfully express Factor IX. In fact, Hao states "[i]t is not known which specific hematopoietic cell type(s) would be best for expression of factor IX." *Id.* Similarly, Romp states that "[t]o date, however, there is no evidence to suggest that factor IX is synthesized by megakaryocytes." (Romp; page 910, left column, second full paragraph.) Romp also discloses that it is not known whether factor IX bound to platelets is functional. (Romp; page 910, left column, last sentence.)

Uzan identifies a promoter region of the GPIIb gene that is necessary to direct the expression of GPIIb itself in megakaryocytic cells, but then merely suggests that this region "could be used to target the expression of heterologous genes in vivo." (Uzan; page 8938, right column, last sentence (emphasis added).) Taking Hao, Romp, and Uzan together, there is no reasonable expectation of successfully obtaining expression of factor IX in megakaryocytes. The addition of Kurachi, which the Office stated teaches " a construct encoding human factor IX wherein the first intron of human factor IX is inserted into the factor IX cDNA," does not cure this defect. Office Action at page 8.

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For the reasons detailed above, Applicants submit that the present invention is non-obvious. However, in order to expedite prosecution, Applicants have amended claims 1 and 9, as suggested by the Examiner during the June 16, 2002 interview, by deleting the phrase "hematopoietic cells" and adding the term "megakaryocytes." In addition, Applicants canceled claims 5-8, rendering the rejection of these claims moot. Applicants also amended claims 2-4 and added new claims 15 and 16 to correct claim dependency. Applicants retain the right to pursue any subject matter not retained by this amendment in a separate application. During the interview of June 16, 2003, it was agreed upon that "having a promoter specific for expression in megakaryocytes would overcome the obviousness rejection." Interview Summary at page 1. Accordingly, Applicants respectfully request that the rejections of claims 1-4 and 9-12 be withdrawn.

New Enablement Rejection

The Office rejected claim 5 under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. Further, the Office stated that while the specification is "enabling for a process for the production of Factor IX in a hematopoietic cell line in vitro, [the specification] does not reasonably provide enablement for a process for the production of Factor IX in hematopoietic cells in vivo (gene therapy)." Office Action at page 9.

Applicants traverse. Claim 5 has been cancelled and therefore the rejection of this claim is moot.

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Conclusion

In view of the foregoing amendments and remarks, Applicant respectfully requests the reconsideration and reexamination of this application and the timely allowance of pending claims 1-4, 9-12, 15, and 16.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: November 4, 2003

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